Tools to implement the World Health Organization End TB Strategy

Addressing common challenges in high and low endemic countries

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Tools to implement the World Health Organization End TB Strategy: Addressing common challenges in high and low endemic countries

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ABSTRACT

Aim: The purpose of this viewpoint is to summarize the advantages and constraints of the tools and strategies available for reducing the annual incidence of tuberculosis (TB) by implementing the World Health Organization (WHO) End TB Strategy and the linked WHO TB Elimination Framework, with special reference to Oman.
Methods: The case-study was built based on the presentations and discussions at an international workshop on TB elimination in low incidence countries organized by the Ministry of Health, Oman, which took place from September 5 to September 7, 2019, and supported by the WHO and European Society of Clinical Microbiology and Infectious Diseases (ESCMID).
Results: Existing tools were reviewed, including the screening of migrants for latent TB infection (LTBI) with interferon-gamma release assays, clinical examination for active pulmonary TB (APTB) including chest X-rays, organization of laboratory services, and the existing centres for mandatory health examination of pre-arrival or arriving migrants, including examination for APTB. The need for public–private partnerships to handle the burden of screening arriving migrants for active TB was discussed at length and different models for financing were reviewed.
Conclusions: In a country with a high proportion of migrants from high endemic countries, screening for LTBI is of high priority. Molecular typing and the development of public–private partnerships are needed.

Introduction

Tuberculosis (TB) is one of the top 10 causes of death worldwide and the most important cause of death from an infectious disease, surpassing HIV/AIDS. In 2018, TB caused an estimated 1.5 million deaths (range 1.4–1.6 million), including 251 000 deaths among HIV-positive persons (WHO, 2019). The severity of national TB epidemiology varies significantly among countries. Worldwide in 2019, there were fewer than 10 new cases per 100 000 population in most high-income countries, 150–400 in most of the 30 high TB burden countries, and above 500 in six countries (WHO, 2019).

The World Health Organization (WHO) End TB Strategy aims to end the global TB epidemic by 2035, reducing global TB incidence and mortality rates by 90% and 95%, respectively, in 2035 when compared to 2015 (WHO, 2014; Uplekar et al., 2015; Lönnroth et al., 2015). In September 2018, the goal of ending TB was elevated to the highest level at the first-ever UN High Level Meeting on TB in New York, which brought together heads of states and governments, who made bold commitments to accelerate the TB response. Oman is a signatory of the UN High-Level Political Declaration on TB (WHO, 2017).

The WHO End TB Strategy was developed in parallel with the Sustainable Development Goals (SDGs), and interventions should be anchored in the SDGs (Lönnroth et al., 2015; Lönnroth and Raviglione, 2016). It has been estimated that one quarter of the world population are latently infected with TB, having a latent TB infection (LTBI) (Houben and Dodd, 2016), and a recent meta-analysis of prevalence surveys confirmed that 20–25% globally have LTBI (Cohen et al., 2019). This is a challenge for both high and low endemic countries, but it is evident that to reach the goal of TB elimination, the reservoir of LTBI has to be eliminated or reduced significantly (WHO, 2015; Petersen et al., 2019; Rosales-Klintz et al., 2019; Centis et al., 2017).

In view of the progress made in several low-incidence countries, the WHO joined forces with the European Respiratory Society to adapt the WHO End TB Strategy and develop a framework for TB elimination in these countries. Take-up of the WHO TB Elimination framework has been slow (Matteelli et al., 2018) and there are few published country experiences, with the exception of Cyprus, Oman, and Latin America (Al Yaquobi et al., 2018).

Oman as a pathfinder to TB elimination

Oman is a low TB incidence country, with an annual incidence rate of less than 5.9 cases per 100 000 population in 2018 (Figure 1). Forty-five percent of the population are migrants from high-incidence countries, i.e. more than 100 cases per year per 100 000 population, accounting for 60% of the annual TB cases (Table 1; Figure 2). However, several studies have indicated that incidence rates based on notified cases may not fully reflect the burden due to under-reporting (Snow et al., 2018; Pandey et al., 2017; Romanowski et al., 2019).

The purpose of this viewpoint is to summarize the advantages and constraints of the tools and strategies available for reducing the annual incidence of TB by implementing the WHO End TB

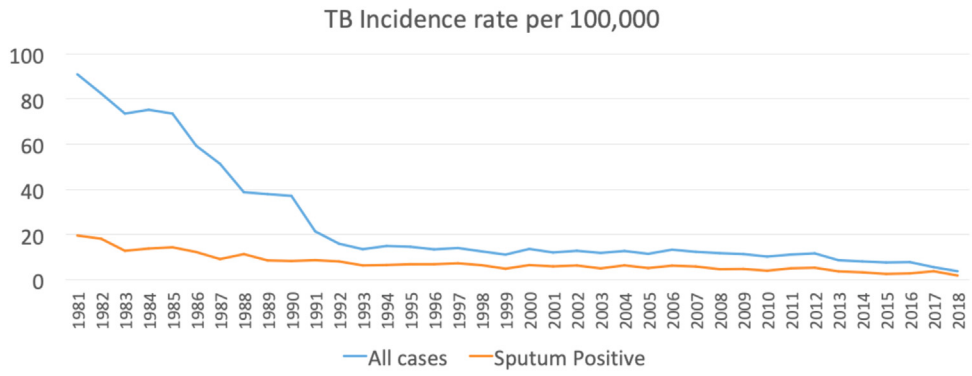

Figure 1. Trend in tuberculosis incidence in Oman—1981–2018.

Table 1
New tuberculosis cases in Omani nationals and migrants.

Year	2010	2011	2012	2013	2014	2015	2016	2017	2018
Omani nationals	214	239	245	188	184	180	190	141	98
Non-Omanis	94	98	141	146	170	147	154	122	145
Nationals per 10^5	10.3	11.2	11.7	8.7	8.1	7.7	6.3	4.7	3.3
Non-nationals per 10^5	8.1	7.1	9.2	8.7	9.8	8.1	7.7	7.1	7.3

Note: Estimated population January 1, 2019: 4 992 364 of which 2994 601 were Omani nationals and 1 997 763 were migrants (National Centre for Statistics and Information).

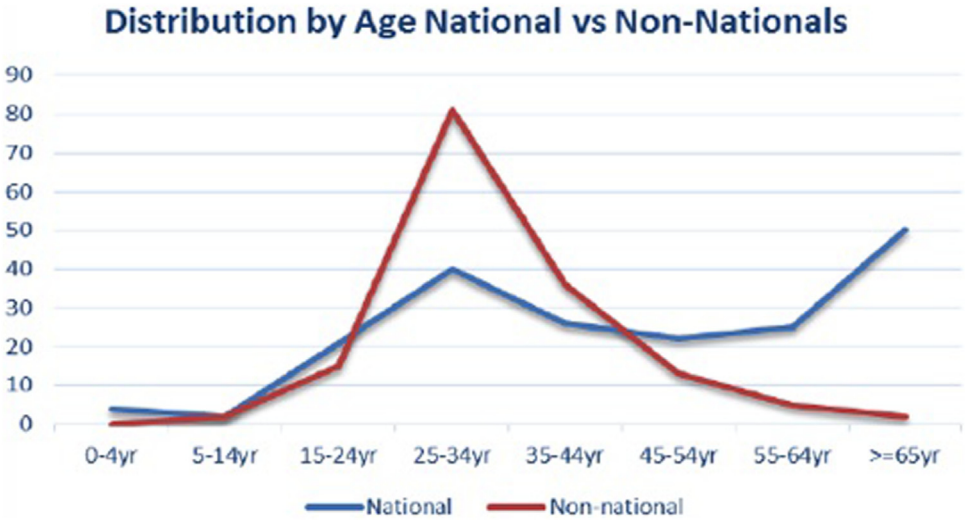

Figure 2. Age-specific annual tuberculosis incidence in Omani nationals and non-Omanis.

Strategy and the linked WHO TB Elimination Framework, with special reference to Oman. In Oman, a reduction in annual TB incidence from 59 per million inhabitants (2018) to 1 per million by 2035 has to be achieved, which is the threshold defining TB elimination (Lönnroth et al., 2015). It may be possible to advance the elimination date if modelling and effective implementation of key interventions, including the roll-out of TB preventive treatment, are conducted.

Methods

The case-study was built based on the presentations and discussions at an international workshop on TB elimination in low incidence countries organized by the Ministry of Health, Oman, which took place from September 5 to September 7, 2019, and supported by the WHO and the European Society of Clinical Microbiology and Infectious Diseases (ESCMID).

The meeting reviewed existing tools, including the screening of migrants for LTBI with interferon-gamma release assays (IGRAs), clinical examination for active pulmonary TB (APTB) including chest X-rays (CXR), the organization of laboratory services, and the existing centres for mandatory health examination of arriving migrants including examination for APTB. The need for public–private partnerships to handle the burden of screening arriving migrants for active TB was discussed at length and different models for financing were reviewed.

The TB elimination framework programme for Oman has opened many topics for applied research. It has also allowed the evaluation of models for public–private partnerships, community support in the treatment LTBI, the evaluation of screening methods for LTBI through long-term follow-up, and comparison of different regimens for the treatment of LTBI, for instance 4 weeks and 12 weeks rifapentin/isoniazid (or rifampicin/isoniazid).

A writing team of global TB experts was invited to summarize the available evidence for the different areas with a non-systematic approach and to discuss this evidence based on Oman-specific data. Several rounds of discussion were organized to reach consensus on the final document.

Background

In 1981, the annual incidence of TB in Oman was over 90 per 100 000 population (Figure 1). Following rapid economic development in the 1980s, the incidence declined significantly to 20 per 100 000 population in 1991 and 10 per 100 000 population in 2010 (Ministry of Health, 2018). Over the same period, the proportion of migrants from high TB endemic countries in Africa and Asia increased to around 45% of the population. Up until 2017, the national policy for TB control was based on the screening of migrants on arrival for APTB with a CXR. Since 2017, investigations for APTB have also included sputum microscopy, culture, and PCR if there is a clinical or radiological suspicion of TB. Pre-arrival screening is also conducted in Gulf Collaboration Council certified centres in the country of origin of migrants for around 90% of the migrants.

The proportions of APTB cases among Omani nationals and non-nationals have been changing, with a decreasing number in Omanis and an increasing number diagnosed in non-Omanis (Table 1). The stable incidence rate for migrants and the slow decrease in rate for Omani nationals over the last 10 years potentially reflect *Mycobacterium tuberculosis* (Mtb) transmission from the migrant population (Aldridge et al., 2016), but that assumption needs to be confirmed by genotyping. TB in migrants comprises either reactivation of LTBI, diagnosed some years after entry, or cases missed by the pre-entry or at-entry screening.

It is often held that new cases of TB that occur some years after entry could be the result of the reactivation of LTBI (Aldridge et al.,

Table 2
Pillars of the End TB strategy.

Integrated, patient-centred care and prevention
1. Early diagnosis of tuberculosis including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups
2. Treatment of all people with tuberculosis including drug-resistant tuberculosis, and patient support
3. Collaborative tuberculosis/HIV activities, and management of comorbidities
4. Preventive treatment of persons at high risk, and vaccination against tuberculosis
Bold policies and supportive systems
5. Political commitment with adequate resources for tuberculosis care and prevention
6. Engagement of communities, civil society organizations, and public and private care providers
7. Universal health coverage policy, and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control
8. Social protection, poverty alleviation and actions on other determinants of tuberculosis
Intensified research and innovation
9. Discovery, development and rapid uptake of new tools, interventions and strategies
10. Research to optimize implementation and impact, and promote innovations

2016; Lillebaek et al., 2001; Lönnroth et al., 2017; Zenner et al., 2017; Kamper-Jørgensen et al., 2012a,b). Previous studies have shown that screening for active TB at entry detects only a small number of TB cases, but will miss cases reactivating after entry if screening for LTBI is not included (Abubakar et al., 2011; Kruijshaar et al., 2013), indicating that screening aimed only at identifying APTB cases at entry may miss an unknown proportion of cases who are developing TB at a later point.

The Ministry of Health has estimated that Oman has to reduce the incidence by around 10% per year to reach the goal of a 90% reduction in the incidence rate by 2035. To reduce the current incidence of 59 cases per million population (Table 1) to less than 1 per million by 2035 will pose significant challenges. The age distribution among non-Omanis is younger than in Omanis, where older cases are likely more commonly due to reactivation of LTBI (Figure 2).

Oman fulfils the first three goals of the pillars of the End TB Strategy (Table 2) and partly also the fourth, "Preventive treatment of persons at high risk, and vaccination against tuberculosis", by including universal bacillus Calmette–Guérin (BCG) immunization at birth and preventive treatment of contacts of known active TB cases. The current strategy does not include the screening of migrants from highly endemic countries for LTBI.

Points 5–8 of the TB Elimination Framework are partly fulfilled in Oman, in that there is political commitment and universal government-funded healthcare coverage and regulatory frameworks for case notification, vital registration, quality and rational use of medicines, and infection control.

Regarding points 9 and 10, regarding 'intensified research and innovation', this paper will discuss the strategies and tools available to reduce the incidence in Oman by 10% per year.

A previous modelling study, which reviewed seven different screening programmes for migrants, found that screening with an IGRA followed by a short regimen (3 months) of either rifampicin/isoniazid or rifapentine/isoniazid was the most cost-effective algorithm in the United Kingdom (Kowada, 2016; Abubakar et al., 2018). Risk groups among Omani nationals need to be identified (Katelaris et al., 2019), for instance the elderly, families with previous TB cases, geographical clustering, and prisons (Noppert et al., 2019). A study from Japan found that overall population density, age, and being a healthcare worker (HCW) were risk factors for TB (Murakami et al., 2019).

Specific interventions for national TB control and elimination programmes in the End TB era

Multisectoral collaboration and political commitment

TB is a disease of poverty and deprivation, which can only be controlled by involving multiple stakeholders and addressing the need of marginalized groups with a high incidence, as recently reviewed by the The Lancet Commission on TB (Reid et al., 2019). The often long incubation period, the latent stage with no symptoms, and the lack of access to proper diagnostics and management hamper control efforts. Political commitment is key to addressing the complex interaction between socio-economic problems and healthcare provision (Matteelli et al., 2018).

One example is the Zero TB Initiative, which creates support for local stakeholders helping to mobilize financial and technical resources. Examples are the mobile units in rural areas of South Africa providing treatment, and mobile CXR units in Karachi, Pakistan (Zero TB Initiative). Such outreach is key to reach marginalized populations and will benefit from a mixture of private funded and public initiatives.

The government will support policies, which inform migrants in their own language of their right to seek medical care, the signs and symptoms of TB, and the right to free treatment in Oman without the risk of being repatriated in the case of APTB. The End TB Strategy was reiterated in the Moscow Declaration adopted at the first WHO Global Ministerial Conference on ending TB in 2017, where ministers of health (Zumla and Petersen, 2018) including the minister for Oman, declared "We reaffirm our commitment to end the TB epidemic by 2030" (WHO, 2017). The Moscow Declaration called for the development of a multisectoral accountability framework, which was reiterated in the UN High Level Meeting Political Declaration by heads of state.

Managing LTBI in migrants

Similar to other countries in the Gulf Cooperation Council, Oman is characterized by a local population with a low incidence of TB and a large population of migrants with a higher incidence of TB. Managing LTBI in this population is a clear priority. The topic was discussed with focus on both screening and diagnostic challenges, as well as on treatment (Shete et al., 2018; Wild et al., 2017; Shedrawy et al., 2017; Zenner et al., 2017; Kunst et al., 2017; Dara et al., 2017). A study from the Netherlands found that the most important predictor for developing active TB was known exposure, but being foreign-born was an independent risk factor (Erkens et al., 2016), and 72% of new TB cases were foreign-born (van de Berg et al., 2017).

Diagnosis of LTBI

Mandatory health examinations of migrants in Oman take place at pre-entry, on arrival, and then every 2–4 years as part of visa renewal. A CXR is included in these medical examinations, potentially identifying cases of APTB.

A pilot study from Oman found that 21% of migrants from Asia and 31% from Africa were IGRA-positive (Yaquobi et al., submitted). Screening for LTBI is usually performed by tuberculin skin test (TST) or IGRA, which both detect cell-mediated immune responses against TB antigens (Getahun et al., 2015; Goletti et al., 2018a,b).

These tests cannot distinguish active TB from LTBI. Even though IGRAs have several advantages compared to TST, they are more expensive, rely on blood sampling, and require a diagnostic laboratory (Pai et al., 2014). In immunocompetent subjects, IGRAs have a very high negative predictive value (NPV; >99%) but as the tests rely on the cell-mediated immune responses, there is a risk of false-negatives from immunosuppression. For the QuantiFERON-TB Gold (QFT) test, there is also increasing awareness that a grey zone range (at least 0.20–0.70 IU/ml) should be used around the cut-off (0.35 IU/ml) to avoid both false-negative results due to recent exposure or immunosuppression and also false-positive results (Pai et al., 2014). It should be noted that the false-negative rate of an IGRA in patients with active TB has been reported to be approximately 12% (Nguyen et al., 2018). Thus IGRA screening for LTBI may not identify all cases of active TB. However, conversely, a study from the UK found that pre-entry screening was strongly and independently associated with fewer APTB cases among new migrants (Berrocal-Almanza et al., 2019).

Management of LTBI in migrants to Oman

A pragmatic approach to reduce TB incidence could be to select the migrants with a strongly positive IGRA of >4 IU/ml and offer them preventive therapy of 3 months of combined rifampicin or rifapentin and isoniazid.

Two studies (Winje et al., 2018; Andrews et al., 2017) found that individuals with a strongly positive (>4 IU/ml) IGRA test had a relative risk of 30 of developing APTB within the next 2 years. A study from the UK found an approximately five-times higher risk compared to baseline for developing APTB in subject with a TST >15 mm, positive T-Spot.TB, or positive IGRA (Abubakar et al., 2018). However, a follow-up study found that higher thresholds for QFT, T-Spot.TB, and TST modestly increased the positive predictive value (PPV) for incident TB, but markedly reduced sensitivity (Gupta et al., 2019).

In 2018, 943 377 migrants were examined in the medical migrant examination centres in Oman, and 33% (311 314) of them were new arrivals. The study of IGRA reactivity in migrants (Yaquobi et al., submitted) showed that 22.4% had a positive IGRA, i.e., 69 734 out of the 311 314 new arrivals. Should all 69 734 receive treatment for latent TB?

Migrants usually stay in Oman for an average of 4 years and it can be argued that with a low or median reactivity (0.35–4 IU/ml) and without known risk factors for developing active TB, the persons should be informed about their status of LTBI and advised to seek treatment at their own expense. However, we could consider prioritizing for treatment only migrants with a strongly positive QFT of >4 IU/ml or those with risk factors (such as immunosuppression) and a positive QFT (>0.35 IU/ml). This strategy would reduce the number of persons offered treatment from 69 734 to 17 224 (24%). This is still a high number, but distributed in the major cities the task should be manageable in a public–private partnership programme.

Extending the service by developing public–private partnerships

In 2018, 3 million of the estimated 10 million people with TB worldwide were 'missed' by national TB programmes (NTPs) (WHO, 2019). Two-thirds of them are thought to access TB treatment of questionable quality from public and private providers who are not engaged by the NTPs. The quality of care provided in these settings is often not known or substandard (WHO, 2019). To close these gaps, the WHO and partners have launched a new roadmap to scale up the engagement of public and private healthcare providers (WHO, 2018). Also in Oman, the future challenges of the TB control programme need resources provided by the private health sector, both in diagnostics and the management of LTBI.

The government is committed to providing treatment for both LTBI and active TB, to both Omani nationals and migrants. This will be done either in public or private facilities.

Involvement of the private sector in the diagnosis and management of LTBI requires a quality control programme for the diagnostic tests used and regular reporting of treatment outcomes, including compliance. The government needs to develop models for cost covering of services – diagnostic and clinical – provided in the private sector within the framework of universal health coverage (UHC), as has already been done successfully in countries such as Pakistan, Bangladesh, India, and Indonesia. UHC means that all people have access to the health services they need, when and where they need them, without financial hardship, and this is part of the SDGs (WHO UHC, 2019). UHC was addressed by a high-level meeting at the United Nations General Assembly (UNGA) on September 23, 2019 (WHO UNGA, 2019). The Oman Minister of Health, at a side event held on multisectoral action to end TB by the WHO and the Russian Federation at the UNGA, stressed the need for greater commitment in reaching vulnerable groups such as migrants. He called for greater partnership across all sectors, including the private sector, to reach this goal.

The private health sector in Oman is capable of and willing to handle screening for LTBI and follow-up treatment. The key is the financial model. There are two options: (1) an insurance paid model where the employer responsible for the migrant worker has insurance that covers the diagnosis and management of LTBI; and (2) a model where the private sector clinics are reimbursed by the government after the price for the service has been negotiated. The incentives that could be offered could include accreditation and positive branding of collaborative private sector health facilities, as well as access to new tools such as rapid diagnostic tests and new drugs that are currently only available in the public sector.

Developing molecular characterization by whole genome sequencing (WGS) to uncover transmission routes and define clusters and detect genotype resistance

A single study from Oman used spoligotyping to explore the genetic population structure and clustering of Mtb isolates among nationals and immigrants (Al-Maniri et al., 2010). The study found a predominance of the strain families commonly found on the Indian sub-continent. A high proportion of immigrant strains were in the same clusters as Omani strains (Al-Maniri et al., 2010). However, spoligotyping has a very low discriminatory power compared to WGS.

Genotyping Mtb strains from TB patients over time provides detailed information on the Mtb transmission dynamics (Folkvardsen et al., 2017; Andrés et al., 2019), and it is possible to determine transmission among and between nationalities (Kamper-Jørgensen et al., 2012a). This information can be used to optimize the public health management of TB, e.g. by directing the TB control efforts to specific risk-groups (Karmakar et al., 2019). A study from Copenhagen found a prevalence rate of APTB of 3% in homeless people identified by sputum culture (Jensen et al., 2015).

Specifically in Oman, WGS will be useful to determine the amount of transmission between migrant workers and Omanis and to identify high-risk groups and hotspots for active TB transmission within the country.

In addition, systematic use of WGS on all Mtb isolates will allow the emergence of drug resistance to be monitored and, if implemented from early liquid culture, could allow the cost of phenotypic drug sensitivity tests on strains that are fully wild-type for first-line drugs to be reduced. This strategy will be fully

compliant with pillar 1: early diagnosis of TB including universal drug-susceptibility testing, and systematic screening of contacts and high-risk groups. The Oman Central Public Health Laboratory has received a grant from the Oman Research Council on "Understanding TB transmission and epidemiology using molecular and geo-spatial methods", and this will be incorporated into the routine surveillance in the future.

Patient-centred care including treatment support

The key challenge with programmatic LTBI screening is compliance with preventive treatment (Frieden and Sbarbaro, 2007; Newell et al., 2006). A recent review of LTBI treatment in migrants found an overall poor level of compliance (Greenaway et al., 2018), and one possibility is to extend the community-based treatment support to cover preventive treatment of LTBI. Adherence to preventive treatment of LTBI infection in Oman was found to be 42% among HCWs (Khamis et al., 2016). During 2 years of community-based care delivery in Muscat Governorate, 18 out of 27 Omani pulmonary TB patients included in 2017 and all Omani nationals with pulmonary TB ($n = 16$) in 2018, except two new cases, were on community-based care delivery. There was a significant reduction in average length of hospital stay for pulmonary TB patients when compared to previous years (27 days in 2017 and 28 days in 2018, compared to 61 days in 2016).

This may help with the acceptability of preventive treatment among recipients and may contribute to reduce in-hospital transmission (Migliori et al., 2019). Even though community preventive treatment support is not presently offered to people with LTBI, some form of support to ensure adherence that is either family or community based would be desirable. This could be enhanced through the use of digital and video technology. To increase compliance, the 3-month course with a rifapentin or rifampicin/isoniazid combination is much preferred.

TB in high-risk groups

Healthcare workers

The United States recently (2019) revised its recommendations for the surveillance of TB in HCWs, because the risk was determined to be very low (Sosa et al., 2019). The new recommendations include baseline (pre-placement) TB screening with an individual risk assessment and symptom evaluation for all personnel, and testing with an IGRA or TST for personnel with known exposure to TB. A recent study from Korea including 3920 HCWs tested with an IGRA found that 893 (22.8%) had LTBI (Han et al., 2019). The study also found that the acceptance rate for treatment of LTBI was 64.6% with 3 months of rifampicin/isoniazid or 4 months of rifampicin.

TB in children

TB cases in Omani children are shown in Table 3. Children pose unique challenges to TB control programmes, as infection in this age group is considered a sentinel event indicating recent transmission.

The importance and priority of children as a special high-risk group was highlighted in the WHO End TB Strategy (WHO, 2014). A recent study estimated that 70% of active TB in children in West Africa is not diagnosed (TDR, 2019).

The main interventions to prevent new cases in children are vaccination with the bacillus Calmette-Guérin (BCG) vaccine, contact tracing and screening for active TB, and treatment of LTBI (Thomas, 2017). BCG immunization has been terminated in many low endemic countries due to more side effects than potentially prevented TB cases. A modelling study of the preventive effect of BCG vaccination found that a 92% BCG coverage at birth reduced TB deaths in the global birth cohort by 2.8% (0.1–7.0%, confidence interval) by age 15 years, and that a 100% coverage at birth reduced TB deaths by 16.5% (0.7–41.9%, CI) (Roy et al., 2019).

The WHO has strongly recommended treatment for LTBI in children under 5 years of age who are household contacts of pulmonary TB cases (WHO, 2018). The performance of screening tests like the TST and IGRA is poorly documented in children below 2 years of age (Box 1).

There is an increasing need for microbiological (culture) confirmation of TB disease, which is limited by the paucibacillary nature of TB in children. Furthermore, the newer rapid molecular tests are positive in the minority of children, generally <25–40% of children with TB disease (WHO, 2013; Jenkins et al., 2014).

Screening algorithms and cost-effectiveness

Current LTBI screening is limited by the relatively low PPV of available tests (Rangaka et al., 2012). Although the PPV appears better for some IGRA tests compared with the TST (Abubakar et al., 2018; Gupta et al., 2019), defining reactivation risk varies significantly by population group. The selection of the population group determines the efficiency and cost-effectiveness of the approach (Zenner et al., 2017). Thus screening those at highest risk of reactivation, such as persons with immunosuppression, is most cost-effective (Greenaway et al., 2018), and this has led to the recommendation to focus on these high-risk groups for LTBI control (WHO, 2017; ECDC, 2018). In the context of TB elimination and the large estimated numbers of persons with LTBI (Houben and Dodd, 2016), strategies need to include further groups.

There is a conditional recommendation for screening of a number of groups, including recent migrants from high incidence countries (WHO, 2017 LTBI guidelines). A way forward is stratification by epidemiological risk factors (country of origin, time since arrival), demographic factors (age groups), co-morbidities, or social risk factors. There is no consensus on thresholds (Greenaway et al., 2018), and practices vary significantly between countries (Kunst et al., 2017). The decision on thresholds will depend on preferences and choices around the population impact of screening, individual risks and benefits, and cost-effectiveness.

Table 3
Tuberculosis cases in children.

Year	Omani	Non-Omani	Total
2010	9	1	10
2011	9	2	11
2012	12	0	12
2013	10	4	14
2014	6	1	7
2015	9	1	10
2016	6	2	8
2017	7	1	8
2018	6	0	6

Box 1. Fact box.

The End TB targets are:

1 A 95% reduction by 2035 in number of TB deaths compared with 2015;
2 A 90% reduction by 2035 in TB incidence rate compared with 2015;
3 Zero TB-affected families facing catastrophic costs due to TB by 2035 (WHO, 2015).

The UK has chosen its incidence threshold of 150 per 100 000 for the LTBI programme based on cost-effectiveness studies (Pareek et al., 2011).

Modelling

Part of the End TB Framework is to empower a strong and self-sustained TB research community in low- and middle-income countries with a high TB burden. In Oman, the next revision of the National TB Strategic Plan will include a national research plan.

The scale of the possible interventions will create a substantial burden, both in terms of financial costs and population or healthcare system impact. It is therefore critical that interventions are designed rationally, and optimized with regards to maximal impact and minimal burdens. Mathematical modelling provides important tools for the assessment of potential strategies, and allows for comparison of a wide range of possible approaches with relatively minimal resource implications.

In the specific context of Oman, mathematical modelling approaches could be used to consider the optimal screening algorithms for latent and active TB in migrants and nationals, and to evaluate the efficiency of different strategies. This could include the selection of the most appropriate tests, testing frequency, and cost-effective approaches to TB incidence reduction. One obvious task for a modelling analysis is to look at active TB in Omani nationals in order to provide data indicating whether screening for latent TB of part of the Omani population would be beneficial. Modelling can identify high-risk groups in the community, whether nationals or migrants.

Research

There is a need for operational research aimed at optimizing the cost-effectiveness of the different interventions, identifying high-risk groups in the community, follow-up of persons with LTBI without treatment, and stratification of the risk of developing active TB based on the strength of the IGRA level or TST reactivity (Goletti et al., 2018b; Kik et al., 2018).

An obvious research project would be to compare 3 months of preventive treatment with 1 month (Swindells et al., 2019). The existing mandatory health investigation including a CXR every 2–4 years will ensure that follow-up is done if the migrant stays in Oman. This will allow studies on the effectiveness and cost-effectiveness of active TB screening in combination with LTBI or LTBI only.

The extension of treatment support services to cover LTBI in order to increase compliance and a general switch from 6 or 9 months of isoniazid to 3 months of rifapentin or rifampicin/isoniazid are needed. The planned screening of migrants with mandatory follow-up every 2 years will also allow Oman to generate data on the efficacy of the screening assay and efficacy of the treatment offered, as it is expected that most active TB cases will develop after arrival.

Models for public–private partnerships to enlarge affordable coverage for all, need to be developed, tried, and validated. A recent study from Australia compared central and decentralized management in TB programmes and concluded that central programmes were better suited to change and challenges (Degeling et al., 2019)

Conclusions

Fulfilling the WHO End TB Strategy and the WHO TB Elimination Framework requires a comprehensive package of strategies. This review of the challenges of achieving TB elimination in a low endemic country like Oman with a high number of migrants from high TB endemic countries, clearly shows that screening for LTBI and the treatment of either all cases with LTBI or high-risk cases, is a key intervention to reduce new cases. In more high-endemic settings, the identification of high-risk groups and screening these for LTBI, followed by preventive treatment, is an initial strategy.

Molecular typing of all new cases in both nationals and migrants is needed to identify clusters and fully understand the transmission chains.

The development of public–private partnerships is needed to handle the burden of screening and treating migrants for LTBI. This requires political decisions and quality control of diagnostics and management in private healthcare facilities. With high-level political commitment in Oman to eliminate TB, the country could be among the first to achieve TB elimination and serve as a pathfinder for the region and the world.

Conflict of interest

The authors declares no conflict of interest.

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